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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/674,702	09/30/2003	Gail K. Buehler	MCP5017	4561

27777 7590 10/27/2010  
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EXAMINER
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SOROUGH, LAYLA

ART UNIT	PAPER NUMBER
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1627

NOTIFICATION DATE	DELIVERY MODE
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10/27/2010

ELECTRONIC

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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<b>Office Action Summary</b>	<b>Application No.</b> 10/674,702	<b>Applicant(s)</b> BUEHLER ET AL.	
	<b>Examiner</b> LAYLA SOROUGH	<b>Art Unit</b> 1627	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 10 August 2010.
- 2a) ☒ This action is **FINAL**.                      2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-6,8-17,19,21 and 23-27 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-6,8-17,19,21 and 23-27 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |   |   |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)                    | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____                                      |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)         | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____   | 6) <input type="checkbox"/> Other: _____                          |

## **DETAILED ACTION**

The response filed August 10, 2010 presents remarks and arguments submitted to the office action mailed May 12, 2010 is acknowledged.

Applicant's arguments over the 35 U.S.C. 103(a) rejection of claims 1-6, 8-17, 19, 21, 23-27 over Gowan, Jr. (US 5374659 A—previously presented), Gergely et al. (US 5834019 A – previously presented), Patel et al. ( US Pat No. 6569463), Eichman (US Pat. No. 5,980,882—previously presented), McNamara et al. (6423298) Hagemann et al. (US Pat 5,211,957– previously presented) and Saeedi et al. (Prevention Of Crystal Growth In Acetaminophen Suspensions By The Use Of Polyvinyl Pyrrolidone Bovine Serum Albumin; DARU Volume 11, No 3, 2003) is not persuasive. Therefore, the rejection of record is herewith maintained.

Applicant's arguments over the 35 U.S.C. 103(a) rejection of claims 1-6, 8-17, 19, 21, 23-27 over Reinhardt et al. (US Pat No. 6,217,998) in view of Hansenne et al. (US Pat No. 6916464 B2),Walch (US Pat No. 6790847), and Patel et al. (US Pat No. 6569463) is not persuasive. Therefore, the rejection of record is herewith maintained.

The rejections of record are modified to address the new limitations:

### ***Claim Objections***

The numbering of claims is not in accordance with 37 CFR 1.126 which requires the original numbering of the claims to be preserved throughout the prosecution. When claims are canceled, the remaining claims must not be renumbered. When new claims are presented, they must be numbered consecutively beginning with the number next following the highest numbered claims previously presented (whether entered or not).

Misnumbered claims 26, 26 have been renumbered 26, 27.

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1-6, 8-17, 19, 21, 23-27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gowan, Jr. (US 5374659 A—previously presented), Gergely et al. (US 5834019 A – previously presented), Patel et al. ( US Pat No. 6569463), Eichman (US Pat. No. 5,980,882—previously presented), McNamara et al. (6423298) Hagemann et al. (US Pat 5,211,957– previously presented) and Saeedi et al. (Prevention Of Crystal Growth In Acetaminophen Suspensions By The Use Of Polyvinyl Pyrrolidone Bovine Serum Albumin; DARU Volume 11, No 3, 2003).

Gowan, Jr. teaches an aqueous pharmaceutical suspension composition comprising an insoluble pharmaceutical active, a suspension stabilizing effective amount of xanthan gum (hydrocolloid and thickener), pregelatinized starch (swelling agent and thickener) and polyoxyethylene sorbitan monooleate (surfactant) (see abstract). The pH of the composition is preferably between 3.5 and 5 (col 5 line 6). Application of the compositions and method of the present invention for medical and pharmaceutical uses can be accomplished by any clinical, medical and pharmaceutical methods and techniques as are presently or prospectively known to those skilled in the

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art. Thus it is intended that the present invention cover the modifications and variations of this invention provided that they come within the scope of the appended claims and their equivalents (col 7 lines 54-61).

The reference fails to teach the active agent- Loratadine, the nucleation inhibitor - PVP, and the amino polycarboxylic acid compound- EDTA.

Gergely et al. is solely used to show that Loratadine is virtually completely water-insoluble and has a very strongly hydrophobic character. It is thus extremely poorly wettable and therefore difficult to suspend. Its fine particles furthermore have the tendency to form a film on the water surface, to creep up the glass wall to a pronounced extent and to adhere relatively strongly there.

Patel et al. teaches "compositions of the present invention can be used for improved delivery of hydrophilic or hydrophobic pharmaceutical active ingredients, such as drugs, nutritional, cosmeceuticals and diagnostic agents (Col 28 line 57-67)." Such pharmaceuticals include loratadine. The pharmaceutical compositions can include one or more additive such as **solubilizers**, i.e., additives to increase the solubility of the pharmaceutical active ingredient (col 29 lines 16-21). The "solid pharmaceutical compositions of the present invention can optionally include one or more additives, sometimes referred to as excipients. The additives can be contained in an encapsulation coat in compositions which include an encapsulation coat, or can be part of the solid carrier, such as coated to an encapsulation coat, or contained within the components forming the solid carrier. Alternatively, the additives can be contained in the pharmaceutical composition but not part of the solid carrier itself (col 28 lines 57-67)."

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Hence reading on the limitation uniformly dispersed nucleation inhibitor of claim 1.

Preferred **solubilizers** for use in the compositions include triacetin, triethylcitrate, ethyl oleate, ethyl caprylate, dimethylacetamide, N-methylpyrrolidone, N-hydroxyethylpyrrolidone, polyvinylpyrrolidone(nucleation inhibitor) (Col 29 line 57-60).

Other additives include enzyme inhibitors and chelating agents such as EDTA. The amounts of additives can be readily determined by one skilled in the art, according to the particular properties desired. Exemplified is a composition comprising 5% w/w solution of polyvinylpyrrolidone.

Additionally, Patel et al. teaches "Spherical particles are preferred, and these may be produced through spheronization or a spherical crystallization process. Crystals or compact granules from dry compaction or extrusion processes, often available commercially, serve as good substrates (col 41 lines 5-10)."

Eichman teaches drug resin complexes stabilized by chelating agents. "The particle size of a resin can differ between two resins." The chelating agent is preferably EDTA (amino polycarboxylic acid compound). EDTA is known to stabilize drugs in solution by retarding their oxidation col 2 lines 60-61). The solution is preferably about 1% EDTA by weight, but may range from about 0.1% to 50%.

McNamara et al. teaches EDTA is used to improve long term storage, surfactants, and suspension stabilizing agents.

Hagemann et al. teaches pharmaceutically acceptable excipients including PVP are, in particular viscosity index improvers which are suitable for stabilizing aqueous suspensions and which inhibit sedimentation (col 4 lines 42-65).

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It would have been obvious to one of ordinary skill in the art to combine the teachings of Gowan, Jr., Gergely et al., Patel et al., Eichman, and Hagemann et al. The motivation to combine the teachings is because (1) Gowan, Jr. teaches an aqueous pharmaceutical suspension composition comprising an insoluble pharmaceutical active, a suspension stabilizing effective amount of xanthan gum (hydrocolloid and thickener), pregelatinized starch (swelling agent and thickener) and polyoxyethylene sorbitan monooleate (surfactant) (see abstract). Application of the compositions and method of the present invention for medical and pharmaceutical uses can be accomplished by any clinical, medical and pharmaceutical methods and techniques as are presently or prospectively known to those skilled in the art. Thus it is intended that the present invention cover the modifications and variations of this invention provided that they come within the scope of the appended claims and their equivalents (col 7 lines 54-61); (2) Gergely et al. teaches Loratadine is virtually completely water-insoluble and has a very strongly hydrophobic character. It is thus extremely poorly wettable and therefore difficult to suspend. Its fine particles furthermore have the tendency to form a film on the water surface, to creep up the glass wall to a pronounced extent and to adhere relatively strongly there., (3) Patel et al., teaches solubilizers for use in the compositions include triacetin, triethylcitrate, ethyl oleate, ethyl caprylate, dimethylacetamide, N-methylpyrrolidone, N-hydroxyethylpyrrolidone, polyvinylpyrrolidone(nucleation inhibitor) (Col 29 line 57-60). Other additives include enzyme inhibitors and chelating agents such as EDTA (4) Eichman teaches drug resin complexes stabilized by chelating agents. "The particle size of a resin can differ between two resins." The chelating

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agent is preferably EDTA (amino polycarboxylic acid compound). EDTA is known to stabilize drugs in solution by retarding their oxidation (col 2 lines 60-61) and (5) Hagemann et al. teaches pharmaceutically acceptable excipients are, in particular viscosity index improvers which are suitable for stabilizing aqueous suspensions and which inhibit sedimentation include PVP (col 4 lines 42-65). A skilled artisan would have reasonable expectation of effectively stabilizing loratadine (antihistamine) a water-insoluble pharmaceutical active.

Gowan, Jr., Gergely et al., Patel et al., and Eichman meet all elemental steps of the instant claims and the compositions created thereof. Since the compositions prepared by Gowan, Jr., Gergely et al., Patel et al., and Eichman meet all elemental components of the instantly prepared composition, they would obviously exhibit the same properties as recited in claims 8-10 and 22. Although the reference teaches within the embodiment of the invention crystalline drug forms are envisaged, whether the drug is in crystal form or amorphous form does not effect the composition. Hence, the various forms are rendered obvious by the teachings of the prior art.

Claims 1-6, 8-17, 19, 21, 23-27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Reinhardt et al. (US Pat No. 6,217,998) in view of Hansenne et al. (US Pat No. 6,916,464 B2), Walch (US Pat No. 6,790,847), and Patel et al. (US Pat No. 6,569,463).



Reinhardt et al. teaches a composition comprising EDTA in 0.05%, xanthan gum, PVP, fillers, and pigments. Prior to application to the sponge the composition of Reinhardt et al. is an aqueous suspension.

The reference fails to teach the pH claimed or the active agent loratadine in crystal form.

Hansenne et al. is solely used for the teaching that “When the physiologically acceptable medium is an aqueous medium, it generally preferably has a pH which is compatible with the skin preferably ranging from 3 to 9 and better still from 3.5 to 7.5.”

Walch teaches a drug composition useful for topical application of antihistamines loratadine which are incorporated with cosmetics and pigments (col 5 lines 5-8).

Patel et al. teaches “compositions of the present invention can be used for improved delivery of hydrophilic or hydrophobic pharmaceutical active ingredients, such as drugs, nutritional, cosmeceuticals and diagnostic agents (Col 28 line 57-67).” Such pharmaceuticals include loratadine. The pharmaceutical compositions can include one or more additive such as **solubilizers**, i.e., additives to increase the solubility of the pharmaceutical active ingredient (col 29 lines 16-21). The “solid pharmaceutical compositions of the present invention can optionally include one or more additives, sometimes referred to as excipients. The additives can be contained in an encapsulation coat in compositions which include an encapsulation coat, or can be part of the solid carrier, such as coated to an encapsulation coat, or contained within the components forming the solid carrier. Alternatively, the additives can be contained in the pharmaceutical composition but not part of the solid carrier itself (col 28 lines 57-67).”

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Hence reading on the limitation uniformly dispersed nucleation inhibitor of claim 1.

Preferred **solubilizers** for use in the compositions include triacetin, triethylcitrate, ethyl oleate, ethyl caprylate, dimethylacetamide, N-methylpyrrolidone, N-hydroxyethylpyrrolidone, polyvinylpyrrolidone(nucleation inhibitor) (Col 29 line 57-60).

Other additives include enzyme inhibitors and chelating agents such as EDTA. The compositions can be formulated for oral, nasal, buccal, ocular, urethral, transmucosal, vaginal, topical or rectal delivery. Additionally, Patel et al. teaches "Spherical particles are preferred, and these may be produced through spheronization or a spherical crystallization process. Crystals or compact granules from dry compaction or extrusion processes, often available commercially, serve as good substrates (col 41 lines 5-10)." The amounts of additives can be readily determined by one skilled in the art, according to the particular properties desired. Exemplified is a composition comprising 5% w/w solution of polyvinylpyrrolidone.

Therefore, a skilled artisan would have reasonable expectation of successfully producing a topical formulation with a local antihistamine effect with the pH claimed. The motivation comes from the teaching of Walch that the antihistamine loratadine is useful for topical application; the composition is incorporated with cosmetics inclusive of pigments; and Hansenne et al. it is generally preferably has a pH which is compatible with the skin preferably ranging from 3 to 9 and better still from 3.5 to 7.5. Hence, a skilled artisan would have had reasonable expectation of successfully producing a composition with similar efficacy and results.

### ***Response to Arguments***

Applicant's arguments filed August 10, 2010 have been fully considered.

Applicant argues, neither Gowan, Gergely et al., Patel et al., Eichman, nor Hagemann et al. disclose the use of from above about 0 to about 5 % weight per volume polyvinylpyrrolidone as a nucleation inhibitor and the use of from about 0.005 to about 0.1% weight per volume of an amino polycarboxylic acid compound to impart improved pH and viscosity stability in a pharmaceutical composition. Examiner states the references in fact do teach such ranges. See modified rejection above.

The arguments are not persuasive and the rejection is made **FINAL**.

Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the mailing date of this final action.

### ***Conclusion***

No claims allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Layla Soroush whose telephone number is (571)272-

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5008. The examiner can normally be reached on Monday through Friday from 8:30 a.m. to 5:00 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreenivasan Padmanabhan, can be reached on (571) 272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/SREENI PADMANABHAN/

Supervisory Patent Examiner, Art Unit 1627